## AMENDMENTS TO THE CLAIMS

1. (currently amended): A compound of the formula:

and the pharmaceutically acceptable salts thereof wherein:

Ar is an aryl group substituted with 0-5 non-interfering substituents[[,]] selected from the group consisting of alkyl, alkenyl, alkynyl, aryl, arylalkyl, acyl, aroyl, heteroaryl, heteroalkyl, heteroalkyl, heteroalkylaryl, NH-aroyl, halo, OR, NR<sub>2</sub>, SR, SOR, SO<sub>2</sub>R, OCOR, NRCOR, NRCONR<sub>2</sub>, NRCOOR, OCONR<sub>2</sub>, RCO, COOR, alkyl-OOR, SO<sub>3</sub>R, CONR<sub>2</sub>, SO<sub>2</sub>NR<sub>2</sub>, NRSO<sub>2</sub>NR<sub>2</sub>, CN, CF<sub>3</sub>, R<sub>3</sub>Si, and NO<sub>2</sub>, wherein each R is independently H, alkyl, alkenyl or aryl or heteroforms thereof, and wherein two of said optional substituents on adjacent positions can be joined to form a fused, optionally substituted aromatic or nonaromatic, saturated or unsaturated ring which contains 3-8 members wherein two adjacent noninterfering substituents can form a fused aromatic or nonaromatic ring;

 $L^2$ -X- $L^1$  is of the formula:

$$\begin{array}{c|c} L^2 \\ \hline \\ N \\ \hline \\ \end{array}$$

L<sup>1</sup> is CO, SO<sub>2</sub> or alkylene (1-4C);

[[and]] L<sup>2</sup> are linkers is alkylene (1-4C) or alkenylene (2-4C) optionally substituted with one or two moieties selected from the group consisting of alkyl, alkenyl, alkynyl, aryl, arylalkyl, acyl, aroyl, heteroaryl, NH-aroyl, halo, OR, NR<sub>2</sub>, SR, SOR, SO<sub>2</sub>R, OCOR, NRCOR, NRCONR<sub>2</sub>, NRCOOR, OCONR<sub>2</sub>, RCO, COOR, alkyl-OOCR, SO<sub>3</sub>R, CONR<sub>2</sub>, SO<sub>2</sub>NR<sub>2</sub>, NRSO<sub>2</sub>NR<sub>2</sub> CN, CF<sub>3</sub>,

and R<sub>3</sub>Si, wherein each R is independently H, alkyl, alkenyl or aryl or forms thereof containing 1-2 O, S and/or N atoms, and wherein two substituents on L<sup>2</sup> can be joined to form a non-aromatic saturated or unsaturated ring that includes 0-3 heteroatoms which are O, S and/or N and which contains 3 to 8 members or said two substituents can be joined to form a carbonyl moiety or an oxime, oximeether, oximeester or ketal of said carbonyl moiety;

n is 0-3:

each R<sup>1</sup> is independently halo, alkyl, heteroalkyl, OCOR, OR, NRCOR, SR, or NR2, wherein R is hydrogen, alkyl, aryl, or forms thereof containing 1-2 O, S and/or N or a noninterfering substituent;

represents a single or double bond;

one Z<sup>2</sup> is CA or CR<sup>2</sup>A; the other Z<sup>2</sup> is CR<sup>3</sup>, CR<sup>3</sup><sub>2</sub>, NR<sup>4</sup> or N; and each R<sup>2</sup>, R<sup>3</sup> and R<sup>4</sup> is independently hydrogen or a noninterfering substituent are independently selected from the group consisting of H, alkyl, alkenyl, alkynyl, aryl, arylalkyl, acyl, aroyl, heteroaryl, heteroalkyl, heteroalkynyl, heteroalkylaryl, NH-aroyl, halo, OR, NR<sub>2</sub>, SR, SOR, SO<sub>2</sub>R, OCOR, NRCOR, NRCONR<sub>2</sub>, NRCOOR, OCONR<sub>2</sub>, RCO, COOR, alkyl-OOR, SO<sub>3</sub>R, CONR<sub>2</sub>, SO<sub>2</sub>NR<sub>2</sub>, NRSO<sub>2</sub>NR<sub>2</sub>, CN, CF<sub>3</sub>, R<sub>3</sub>Si, and NO<sub>2</sub>, wherein each R is independently H, alkyl, alkenyl or aryl or forms thereof containing 1-2 O, S and/or N and two of R<sup>2</sup> and/or R<sup>3</sup> on adjacent positions can be joined to form a fused, optionally substituted aromatic or nonaromatic, saturated or unsaturated ring which contains 3-8 members, or R<sup>2</sup> and/or R<sup>3</sup> is =O or an oxime, oximeether, oximeester or ketal thereof;

Z³ is NR⁵ or O; where R⁵ is hydrogen or a noninterfering substituent H or is optionally substituted alkyl, alkenyl, alkynyl, aryl, arylalkyl, acyl, aroyl, heteroaryl, heteroalkyl, heteroalkyl, heteroalkyl, heteroalkyl, or is SOR, SO₂R, RCO, COOR, alkyl-COR, SO₃R, CONR₂, SO₂NR₂, CN, CF₃, NR₂, OR, alkyl-SOR, alkyl-SO₂R, alkyl-OCOR, alkyl-COOR, alkyl-COOR, alkyl-CONR₂, or R₃Si, wherein each R is independently H, alkyl, alkenyl or aryl or forms thereof containing 1-2 O, S and/or N;

A is  $-W_i$ - $COX_jY$ , where Y is  $COR^6$  or an isostere thereof, each of W and X is a spacer substituted or unsubstituted alkylene or alkenylene, each of 2-6Å; each of i and j is independently 0 or 1; and  $R^6$  is a noninterfering substituent H, or is straight or branched chain alkyl, alkenyl,

alkynyl, aryl, arylalkyl, heteroalkyl, heteroaryl, or heteroarylalkyl, each optionally substituted with halo, alkyl, heteroalkyl, SR, SOR, SO<sub>2</sub>R, SO<sub>2</sub>NR<sub>2</sub>, OR, NR<sub>2</sub>, OCOR, NRCOR, NRCONR<sub>2</sub>, NRSO<sub>2</sub>R, NRSO<sub>2</sub>NR<sub>2</sub>, OCONR<sub>2</sub>, CN, COOR, CONR<sub>2</sub>, COR, or R<sub>3</sub>Si wherein each R is independently H, alkyl, alkenyl or aryl or forms thereof containing 1-2 O, S and/or N, or

wherein R<sup>6</sup> is OR, NR<sub>2</sub>, SR, NRCONR<sub>2</sub>, OCONR<sub>2</sub>, or NRSO<sub>2</sub>NR<sub>2</sub>, wherein each R is independently H, alkyl, alkenyl or aryl or the heteroatom-containing forms thereof, and wherein two R attached to the same atom may form a 3-8 member carbocyclic or heterocyclic ring and wherein said ring may further be substituted by alkyl, alkenyl, alkynyl, aryl, arylalkyl, heteroalkyl, heteroaryl, heteroarylalkyl, each optionally substituted with halo, SR, OR, NR<sub>2</sub>, OCOR, NRCOR, NRCONR<sub>2</sub>, NRSO<sub>2</sub>R, NRSO<sub>2</sub>NR<sub>2</sub>, OCONR<sub>2</sub>, or R<sub>3</sub>Si wherein each R is independently H, alkyl, alkenyl or aryl or forms thereof containing 1-2 O, S and/or N wherein two R attached to the same atom may form a 3-8 member ring, optionally substituted as above defined.

- 2. (canceled)
- 3. (original): The compound of claim 1 wherein Y is an isostere of  $COR^6$ .
- 4. (original): The compound of claim 3 wherein Y is tetrazole; 1,2,3-triazole; 1,2,4-triazole; or imidazole.
  - 5. (original): The compound of claim 1 wherein each of i and j is 0.
  - 6. (currently amended): The compound of claim [[2]]  $\underline{1}$  wherein j is 0.
  - 7. (original): The compound of claim 1 wherein  $Z^3$  is  $NR^5$ .
  - 8. (canceled)
- 9. (currently amended): The compound of claim [[8]]  $\underline{1}$  wherein  $R^5$  is H, or is optionally substituted alkyl or acyl.

Application No.: 09/989,991

Docket No.: 219002029100

- 10. (canceled)
- 11. (canceled)
- 12. (currently amended): The compound of claim [[11]] wherein R<sup>2</sup> and R<sup>3</sup> are independently selected from halo, OR and alkyl.

5

- 13-38. (canceled)
- 39. (previously presented): The compound of claim 1 wherein the compound is:

- 40. (original): The compound of claim 1 wherein  $L^1$  and  $L^2$  are independently selected from CO, CHOH, CH<sub>2</sub>-NH-CO, CH<sub>2</sub>-N-CH3, and CH<sub>2</sub>.
  - 41. (original): The compound of claim 40 wherein  $L^1$  and/or  $L^2$  is CO.
  - 42. (original): The compound of claim 41 wherein  $L^1$  and/or  $L^2$  is  $CH_2$ -NH-CO.
- 43. (previously presented): The compound of claim 41 wherein  $L^1$  and/or  $L^2$  is  $CH_2$ -N- $CH_2$ .
  - 44. (canceled)
- 45. (currently amended): The compound of claim [[44]]  $\underline{1}$  wherein  $L^2$  and/or  $L^1$  is unsubstituted alkylene.

- Docket No.: 219002029100
- 46. (currently amended): The compound of claim [[44]]  $\underline{1}$  wherein  $L^2$  and/or  $L^1$  is unsubstituted methylene, or methylene substituted with alkyl.
  - 47. (canceled)
- 48. (currently amended): The compound of claim [[47]]  $\underline{1}$  wherein Ar is optionally substituted phenyl.
- 49. (original): The compound of claim 48 wherein said optional substitution is by halo, OR, or alkyl.
- 50. (original): The compound of claim 49 wherein said phenyl is unsubstituted or has a single substituent.
  - 51. (canceled)
  - 52. (currently amended): The compound of claim [[51]]  $\underline{1}$  wherein  $R^1$  is halo or alkoxy.
  - 53. (original): The compound of claim 52 wherein n is 0, 1 or 2.
- 54. (original): The compound of claim 1 wherein  $L^1$  is coupled to the  $\alpha$  ring at the 4-, 5- or 6-position.
  - 55. (original): The compound of claim 1 wherein  $Z^2$  at position 3 is CA or CHA.
  - 56. (original): The compound of claim 55 wherein the Z<sup>2</sup> at position 2 is CR<sup>3</sup> or CR<sup>3</sup><sub>2</sub>.
- 57. (currently amended): The compound of claim 56 wherein R<sup>3</sup> is hydrogen, or is alkyl, alkenyl, alkynyl, aryl, arylalkyl, acyl, aroyl, heteroaryl, heteroalkyl, heteroalkenyl, heteroalkynyl, heteroalkylaryl, NH-aroyl, halo, OR, NR<sub>2</sub>, SR, SOR, SO<sub>2</sub>R, OCOR, NRCOR, NRCONR<sub>2</sub>, NRCOOR, OCONR<sub>2</sub>, RCO, COOR, alkyl-OOR, SO<sub>3</sub>R, CONR<sub>2</sub>, SO<sub>2</sub>NR<sub>2</sub>, NRSO<sub>2</sub>NR<sub>2</sub>, CN, CF<sub>3</sub>,

Application No.: 09/989,991 7 Docket No.: 219002029100

R<sub>3</sub>Si, and NO<sub>2</sub>, wherein each R is independently H, alkyl, alkenyl or aryl or <u>forms thereof</u> <u>containing 1-2 O, S and/or N</u> <u>heteroforms thereof</u> and two of R<sup>1</sup> can be joined to form a fused, optionally substituted aromatic or nonaromatic, saturated or unsaturated ring which contains 3-8 members.

- 58. (currently amended): The compound of claim 57 wherein each R<sup>3</sup> is selected from the group consisting of H, alkyl, acyl, aryl, arylalkyl, heteroalkyl, heteroaryl, halo, OR, NR<sub>2</sub>, SR, NRCOR, alkyl-OOR, RCO, COOR, and CN, wherein each R is independently H, alkyl, or aryl or forms thereof containing 1-2 O, S and/or N heteroforms thereof.
  - 59. (original): The compound of claim 55 wherein  $Z^2$  at position 2 is N or  $NR^4$ .
- 60. (currently amended): The compound of claim 59 wherein R<sup>4</sup> is H, or alkyl, alkenyl, alkynyl, aryl, arylalkyl, acyl, aroyl, heteroaryl, heteroalkyl, heteroalkynyl, heteroalkylaryl, or is SOR, SO<sub>2</sub>R, RCO, COOR, alkyl-COR, SO<sub>3</sub>R, CONR<sub>2</sub>, SO<sub>2</sub>NR<sub>2</sub>, CN, CF<sub>3</sub>, or R<sub>3</sub>Si wherein each R is independently H, alkyl, alkenyl or aryl or forms thereof containing 1-2 O, S and/or N heteroforms thereof.
  - 61. (original): The compound of claim 1 wherein represents a double bond.
  - 62. (canceled)
- 63. (previously presented): A pharmaceutical composition for treating conditions characterized by enhanced p38-α activity which composition comprises
- a therapeutically effective amount of a compound of claim 1 and a pharmaceutically acceptable excipient.
- 64. (original): The composition of claim 63 which further contains an additional therapeutic agent.

Application No.: 09/989,991 8 Docket No.: 219002029100

65. (original): The composition of claim 64 wherein said additional therapeutic agent is a corticosteroid, a monoclonal antibody, or an inhibitor of cell division.

- 66. (previously presented): A method to treat a condition mediated by p38-α kinase comprising administering to a subject in need of such treatment a compound of claim 1 or a pharmaceutical composition thereof.
- 67. (original): The method of claim 66 wherein said condition is a proinflammation response.
- 68. (original): The method of claim 67 wherein said proinflammation response is multiple sclerosis, IBD, rheumatoid arthritis, rheumatoid spondylitis, osteoarthritis, gouty arthritis, other arthritic conditions, sepsis, septic shock, endotoxic shock, Gram-negative sepsis, toxic shock syndrome, asthma, adult respiratory distress syndrome, stroke, reperfusion injury, CNS injury, psoriasis, restenosis, cerebral malaria, chronic pulmonary inflammatory disease, silicosis, pulmonary sarcosis, a bone resorption disease, graft-versus-host reaction, Crohn's Disease, ulcerative colitis, Alzheimer's or pyresis.